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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,477	09/11/2006	Charles Y.F. Young	07039-489US1	9361

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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
09/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/567,477	YOUNG, CHARLES Y.F.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on April 21, 2008.

Status of Claims

Cancellation of claims 3-40 is acknowledged.

Claims 1-2 are currently pending and are the subject of this office action.

Claims 1-2 are currently under examination.

Priority

The present application is a 371 of PCT/US04/25336 filed on 08/04/2004, and claims priority to provisional application No. 60/492,367 filed on o8/04/2003.

Response to Arguments

This is in response to applicant's arguments, filed on April 21, 2008.

Claims rejected under 35 USC 103 (a)

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that: "the present invention is directed towards the discovery of the mechanism of action of NSAIDs (non-steroidal anti-inflammatory drugs) with respect to inhibiting the proliferation of prostate cells. In identifying that mechanism, which is attributed to, in addition to the expression of the androgen receptor, the transactivating ability and/or the IL6-mediated activation of the androgen receptor, the present inventors have provided for methods of screening for NSAID that are effective for inhibiting the proliferation of prostate cancer cells". Applicant also argues that the claimed method is not obvious over the combination of prior art and that the examiner has not articulated any reasoning to support the legal conclusion of obviousness.

First, the active step of monitoring the proliferation of prostate cancer cells in the presence of NSAIDs by determining the level of expression, the transactivating ability, and/or the IL-6-mediated activation of an androgen receptor, will be obvious to the skilled in the art, since Helmbrook et. al. (US 2002/0042375, cited in previous office

action) teach the use of NSAIDs (see abstract and page 1, paragraphs [0002] and [0003]), and Kim et. al. (American Journal of Pathology (2002) 160:219-226) teach that the reduction of the level of expression of the Androgen Receptor (AR) is directly correlated to a decreased cell volume, apoptosis and decline in serum prostate-specific antigen (PSA, a well known marker for prostate cancer) (see page 219, from left column, last three lines through right column, first two lines). In other words, it will be obvious to monitor the level of expression of the AR and correlate it to the effectiveness of any prostate cancer treatment (including castration of nude mice as taught by Kim et. al., or by treatment with NSAIDs as in the instant application), regardless of the mechanism of action.

Second, the discovery of a mechanism of action of a known or obvious process is irrelevant for patentability purposes, because this mechanism of action (i.e. inhibition of the transactivating ability, and/or the IL-6 mediated activation of the androgen receptor by NSAIDs) would have necessarily been present in the method made taught by Helmbrook et. al. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer". The explanation of an effect or mechanism of action obtained when using a compound (e.g. inhibiting expression of AR by NSAIDs) cannot confer novelty on a known process (treating prostate cancer patients or cells with NSAIDs) if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. Though new properties of a compound or their mechanism of action are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability is based upon the therapeutic applications and effects of the compounds, not the mechanism or properties by which they exert such a therapeutic effect.

Rejection under 35 USC 103(a) is maintained.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Helmbrook et. al. (US 2002/0042375) in view of Kim et. al. (American Journal of Pathology, 2002, 160:219-226).

Claim 1 recites a method for monitoring the proliferation of cultured prostate cancer cells in the presence of NSAID, comprising: contacting the prostate cancer cells with one or more NSAID; and determining the level of expression, the transactivation ability, and/or the IL6-mediated activation of an androgen receptor.

Helmbrook et. al. teach a method for treating prostate cancer, which comprises administering to a patient in need thereof at least one non-steroidal anti-inflammatory agent (NSAID) and at least one compound which is a PSA conjugate (see abstract and page 1, paragraphs [0002] and [0003]). Helmbrook et. al. do not teach determining the level of expression of an androgen receptor. However, Kim et. al teach a quantitative method of determining the level of expression of an androgen receptor in CWR22 human prostate cancer xenograft model using video image analysis, to better understand its role in prostate cancer recurrence after castration (see page 219, first column, first sentence; column 2, first sentence of second paragraph, and page 220, column 1, lines 3-8). Kim et. al. further teach that the expression of the AR is directly correlated to the progress of prostate cancer (see page 219, from left column, last three lines through right column, first two lines). At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings of Helmbrook et. al. (contacting the prostate cancer cells with one or more NSAID) and Kim et. al. (determining the level of expression of androgen receptor in prostate cancer cells to better understand its role in prostate cancer recurrence after castration), with the motivation of better monitoring the development of prostate cancer in an individual, thus resulting in the practice of claim 1 with a reasonable expectation of success.

The statement in claim 1: "wherein a decrease in expression, the transactivating ability, and/or the IL6-mediated activation of the androgen receptor indicates an inhibitory activity effect by the NSAID on the proliferation of cancer cells" is considered a characteristic (i.e. it was already present in the prior art, even though the prior art did not recognized it at that time) of the method taught by Helmbrook et. al. (treating prostate cancer with NSAIDs). Although the prior art is silent regarding reducing AR levels by NSAIDS, it seems that applicant has discovered a new mechanism of action of NSAIDs. This of a mechanism of action would have necessarily been present in the method made obvious by Helmbrook et. al. and Kim et. al. In other words, products of identical or similar composition cannot exert mutually exclusive properties when

administered under the same circumstances. MPEP 2112 I states: "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer". The explanation of an effect or mechanism of action obtained when using a compound (e.g. inhibiting expression of AR by NSAIDs) cannot confer novelty on a known process (treating prostate cancer patients or cells with NSAIDs) if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. Though new properties of a compound or their mechanism of action are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability is based upon the therapeutic applications and effects of the compounds, not the mechanism or properties by which they exert such a therapeutic effect.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Helmbrook et. al. (US 2002/0042375) and Kim et. al. (American Journal of Pathology, 2002, 160:219-226) as applied to claim 1 above, and further in view of Nakao et. al. (US 2002/0107273).

Claim 2 recites the same limitations as claim 1, wherein the NSAIDs are celecoxib and/or nimesulide. Helmbrook et. al. and Kim et. al. teach all the limitations of claim 2, except for the specific NSAIDs celecoxib and/or nimesulide. However, Nakao et. al. teach the NSAIDs nimesulide and celecoxib (see page 47, paragraph [0573]). At the time of the invention, it would have been prima facie obvious for a person of ordinary skill in the art to combine the teachings of Helmbrook et. al. (contacting the prostate cancer cells with one or more NSAID) and Kim et. al. (determining the level of expression of androgen receptor in prostate cancer cells to better understand its role in the treatment of prostate (ie.g. castration) with the teachings of Nakao et. al. (NSAIDs nimesulide and celecoxib), with the motivation of monitoring the development of prostate cancer in an individual with well known NSAIDs, thus resulting in the practice of claim 2 with a reasonable expectation of success.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1611
September 8, 2008

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615